

What is claimed is:

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1 1. An injectable pharmaceutical composition comprising:
2 an aqueous suspension of microdroplets suitable for intravenous delivery, the
3 microdroplets having a mean diameter between 200 Angstroms and one micron, the
4 microdroplets comprising a substantially water-insoluble, pharmacologically acceptable
5 liquid, a camptothecin dissolved in the water-insoluble, pharmacologically acceptable liquid,
6 and an outer layer comprising a phospholipid.

1 2. An injectable pharmaceutical composition according to claim 1 wherein the
2 camptothecin is selected from the group consisting of 9-nitro-20(S)-camptothecin, 9-amino-
3 20(S)-camptothecin, 9-methyl-camptothecin, 9-chloro-camptothecin, 9-flouro-camptothecin,
4 7-ethyl camptothecin, 10-methyl-camptothecin, 10-chloro--camptothecin, 10-bromo-
5 camptothecin, 10-fluoro-camptothecin, 9-methoxy-camptothecin, 11-fluoro-camptothecin, 7-
6 ethyl-10-hydroxy camptothecin, 10,11-methylenedioxy camptothecin, and 10,11-
7 ethylenedioxy camptothecin, and 7-(4-methylpiperazinomethylene)-10,11-methylenedioxy
8 camptothecin.

1 3. An injectable pharmaceutical composition according to claim 1 wherein the
2 camptothecin is selected from the group consisting of 9-nitro-20(S)-camptothecin, 9-amino-
3 20(S)-camptothecin, 7-ethyl-10-(4-(1-piperdino)-1-piperdino)-carbonyloxy-camptothecin, 7-
4 ethyl-10-hydroxy-20(S)-camptothecin, 10,11-methylenedioxy-20(S)-camptothecin, 9-chloro-
5 20(S)-camptothecin, 9-bromo-20(S)-camptothecin, 9-hydroxy-20(S)-camptothecin, and 11-
6 hydroxy-20(S)-camptothecin.

1 4. An injectable pharmaceutical composition according to claim 1 wherein the
2 camptothecin is 9-nitro-20(S)-camptothecin.

1 5. An injectable pharmaceutical composition according to claim 1 wherein the
2 pharmaceutical composition has a pH less than 7.

1 6. An injectable pharmaceutical composition according to claim 1 wherein the
2 pharmaceutical composition has a pH less than 6.

1 7. An injectable pharmaceutical composition according to claim 1 wherein the
2 pharmaceutical composition has a pH between 5 and 6.

1 8. An injectable pharmaceutical composition according to claim 1 wherein the
2 pharmaceutical composition comprises an isotonic solution.

1 9. An injectable pharmaceutical composition according to claim 1 wherein the
2 pharmaceutical composition comprises mannitol or trehalose.

1 10. An injectable pharmaceutical composition according to claim 1 wherein the
2 composition has been thermally sterilized.

1 11. An injectable pharmaceutical composition according to claim 1 wherein the
2 composition has been thermally sterilized by heating to at least 121°C for at least 15
3 minutes.

1 12. An injectable pharmaceutical composition according to claim 1 wherein the
2 pharmaceutically acceptable organic liquid is selected from the group consisting of alkanes,
3 dialkyl ethers, long-chain esters, hydrophobic esters, biocompatible silicones, biocompatible
4 high molecular weight fluorocarbons, oil-soluble vitamins and volatile liquid anesthetics.

1 13. An injectable pharmaceutical composition according to claim 1 wherein the
2 camptothecin is present in amounts of up to about 25% w/w.

1 14. An injectable pharmaceutical composition according to claim 1 wherein the
2 camptothecin is present in amounts of from about 0.05% w/w to about 5% w/w.

1 15. An injectable pharmaceutical composition according to claim 1 wherein the
2 camptothecin is present in amounts of from about 0.1% w/w to about 1% w/w.

1 16. An injectable pharmaceutical composition according to claim 1 wherein the
2 camptothecin is present in amount of about 0.2% w/w.

1 17. An injectable pharmaceutical composition according to claim 1 wherein the
2 camptothecin is present in amounts of up to about 5% w/w.

1 18. An injectable pharmaceutical composition comprising:
2 a dispersion in an aqueous carrier solution comprising one or more pharmaceutically
3 acceptable tonicity modifier agents and liquid droplets of micrometer to submicrometer, the
4 droplets comprising
5 a substantially water-insoluble, pharmaceutically acceptable lipophilic liquid vehicle
6 a camptothecin dissolved in the lipophilic liquid vehicle, and
7 an outer layer surrounding the droplet comprising at least one membrane-forming
8 amphipathic lipid,
9 wherein upon thermal sterilization the dispersion does not aggregate, flocculate,
10 agglomerate, or coalesce, and the droplets do not grow in size above a volume weighted
11 mean diameter of 10 μ m.

1 19. An injectable pharmaceutical composition comprising:
2 an aqueous carrier solution comprising one or more pharmaceutically acceptable
3 tonicity modifier agents;
4 a dispersion of liquid droplets of a first size distribution, the liquid droplets
5 comprising
6 a substantially water-insoluble, pharmaceutically acceptable lipophilic liquid
7 vehicle,
8 solid particles of a camptothecin of a second size distribution, and
9 an outer layer surrounding the droplet comprising at least one membrane-
10 forming amphipathic lipid;
11 wherein the first size distribution is in the range of submicrometer to micrometers,
12 and the second size distribution is smaller than the first size distribution; and
13 wherein upon thermal sterilization, the dispersion does not aggregate, flocculate,
14 agglomerate, or coalesce, and the droplets do not grow in size above a volume weighted
15 mean diameter of 10 μ m.

1 20. An injectable pharmaceutical composition according to claim 18 wherein the
2 membrane-forming amphipathic lipid comprises a phospholipid.

1 21. An injectable pharmaceutical composition according to claim 20 wherein the
2 phospholipid is selected from the group consisting of saturated phospholipids, unsaturated
3 phospholipids, synthetic phospholipids, natural phospholipids, and combinations thereof.

1 22. An injectable pharmaceutical composition according to claim 20 wherein the
2 phospholipid is selected from the group consisting of natural and synthetic lipids, hen egg-
3 derived phospholipid, egg phospholipid, purified egg phospholipid, soy phospholipid,
4 dimyristoyl lecithin, didodecanoyl lecithin, dioleoyl lecithin, dilinoleoyl lecithin, alpha-
5 palmito-beta-oleoyl lecithin, alpha-palmitoyl-beta-linoleoyl lecithin, alpha-oleoyl-beta-
6 palmitoyl lecithin, diarachidonyl lecithin, alpha-palmito-beta-myristoyl lecithin, dimyristoyl
7 phosphatidic acid, dipalmitoyl phosphatidic acid, distearoyl phosphatidic acid, phosphatidyl
8 serine, phosphatidyl inositol, dimyristoyl phosphatidyl glycerol, dipalmitoyl phosphatidyl
9 glycerol, dioctadecanoyl phosphatidyl ethanolamine, dioleoyl phosphatidyl ethanolamine,
10 dihexadecyl phosphatidyl ethanolamine, dilauryl phosphatidyl ethanolamine, dimyristoyl
11 phosphatidyl ethanolamine, dipalmitoyl phosphatidyl ethanolamine, Lipoid E80, Lipoid ES,
12 Lipoid 90H, and Lipoid 100H.

1 23. An injectable pharmaceutical composition according to claim 20 wherein the
2 phospholipid comprises Lipoid E80.

1 24. An injectable pharmaceutical composition according to claim 18 wherein the
2 outer layer further comprises cholesterol.

1 25. An injectable pharmaceutical composition according to claim 18 wherein the
2 membrane-forming amphipathic lipid is present in amounts of from 0.2% w/w to about 5%
3 w/w.

1 26. An injectable pharmaceutical composition according to claim 18 wherein the
2 membrane-forming amphipathic lipid is present in amounts of from 1% w/w to about 5%
3 w/w.

1 27. An injectable pharmaceutical composition according to claim 18 wherein the
2 membrane-forming amphipathic lipid is present in amounts of about 4% w/w.

1 30. An injectable pharmaceutical composition according to claim 18 wherein the
2 lipophilic liquid and the membrane-forming amphipathic lipid further comprise cholesterol.

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